REMARKS

Applicants filed Amendment B on September 22, 2003 in response to the Final Rejection of July 22, 2003. Thereafter, the Examiner issued an Advisory Action on October 31, 2003. Applicants are filing herewith a RCE to enter Amendment B and the arguments made therein. This amendment is in furtherance of Amendment B and is intended to specifically address those issued raised in the Advisory Action.

I. Reference to Disclosure

In the Advisory Action, the Examiner objects to Amendment B stating that no reference is made in the amendment for support for the claim amendments. Applicants have the following response to this objection by the Examiner:

Claims 1, 3, 4, 19, 21, 22, and 31 were amended in Amendment B to claim medicaments or other pharmaceutical compositions consisting of a halogenated xanthene as the active component. Such amendments were made to bring these claims into conformance with the specification, which clearly describes such medicaments or other pharmaceutical compositions consisting of a single halogenated xanthene as the active component. Examples in support of such claimed medicaments or other pharmaceutical compositions are found, for instance, in paragraphs 36-39 of the specification as follows:

> "[0036] ... liver cell tumor cells injected into the flanks of nude mice ... resulted in the formation of primary tumors ... at the injection site.... Intratumoral (*i.t.*) and peritumoral (*p.t.*) injection of a 10% solution of Rose Bengal (50 μL of 10% Rose Bengal in saline) resulted in marked red staining of the tumor and the surrounding flank. Within 7 days this Rose Bengal cleared from normal tissue, but the tumor tissue remained stained. Over a period of several

> weeks the previously rapidly growing tumor exhibited stasis, with no significant change in tumor volume and a marked absence of mitotic figures (*e.g.*, exhibiting only non-hyperproliferative cells).
> "[0037] Further, peritumoral injection alone ... of the above Rose Bengal exhibited no detectable retention in normal tissue after 24 hours. Notably, no significant effect ... was noted upon peritumoral injection alone.
> "[0038] Hence, the administered Rose Bengal in these examples not only exhibited selective, persistent accumulation in tumor tissue, but this accumulated agent also exhibits chemotherapeutic efficacy with minimal or no measurable side effects in healthy tissue.
> "[0039] This chemotherapeutic effect ... is further illustrated by the following example. An adult, female dog with a naturally-occurring, recurrent aggressive sarcoma tumor (approximately 20 cc in volume) was treated by injection of approximately 5 cc of a 10% solution of Rose Bengal at several locations throughout the tumor volume. After a period of five days, a follow-up examination of the animal indicated a measurable decrease in tumor density along with significant edema and apparent necrosis of large sections of the tumor. Another follow-up examination after 19 days indicated a further measurable decrease in tumor size. Such a response is indicative of chemotherapeutic activity of the injected Rose Bengal within the tumor mass. It is also notable that no significant side-effects were noted in the healthy tissue surrounding the tumor."

Accordingly, this passage illustrates that a chemotherapeutic medicament or other pharmaceutical chemotherapeutic composition consisting of a halogenated xanthene (in this case Rose Bengal) as the sole active component exhibits the claimed chemotherapeutic properties.

Similar support for these amendments is found in paragraph 43 in the specification (and Figures 3 and 4 referenced therein). For instance, this passage notes that chemotherapeutic compositions consisting of either Rose Bengal or Erythrosin B (both of which are halogenated xanthenes) as the active component exhibit chemotherapeutic properties when tested in vitro:

> "[0043] The inventors tested this hypothesis by evaluating the chemotherapeutic properties of Rose Bengal and Erythrosin B on

> cultures of the bacterium *Staphylococcus aureus*. These data are illustrated in FIGURES 3 and 4. In both illustrations, test cultures were exposed to the indicated agents at the indicated concentrations for the indicated times.... FIGURE 3 illustrates the cytotoxic effects of a 90 minute exposure of *S. aureus* to either Rose Bengal or Erythrosin B. In this figure, Rose Bengal exhibits a marked chemotherapeutic response that is concentration dependent, while Erythrosin B exhibits no significant chemotherapeutic response for this brief exposure duration over the range of concentrations tested. FIGURE 4 illustrates the cytotoxic effects on *S. aureus* for various durations of exposure to Rose Bengal or Erythrosin B.... These data show that the chemotherapeutic properties of the halogenated xanthenes are dependent on exposure time. Notably, the negative slopes for the trend lines of both agents are indicative of cumulative cytotoxicity that is time dependent. The shallower slope for Erythrosin B indicates lower cytotoxicity in this model (e.g. *S. aureus*), consistent with the results illustrated in FIGURE 3."

Thus, this passage clearly demonstrates that halogenated xanthenes other than Rose Bengal (i.e., Erythrosin B in this example) exhibit significant chemotherapeutic properties, thereby supporting the Applicants' amended independent Claims 1, 19 and 31 in Amendment B.

II. Intended Use

The Examiner also argues that the terms "chemotherapeutic" and "therapeutic" are intended use limitations. Applicants respectfully disagree.

Independent Claim 1 is directed to a chemotherapeutic medicament consisting of a halogenated xanthene as the active component, wherein said chemotherapeutic medicament is for chemotherapeutic treatment of diseases of human and animal tissue. The term "chemotherapeutic medicament" is not an intended use but is an actual limitation of the claim. As explained in depth in Amendment B, a chemotherapeutic medicament is a well known term and drug to those skilled in the art. It is a thing and has a specific meaning to those skilled in the art. As explained in

Amendment B, a chemotherapeutic medicament is a clearly different thing to those skilled in the art than the photosensitizers in the cited references. Hence, this is a term which breaths life into the claim and therefore, recognized under well established law as a limitation of the claim.

As discussed in depth in Amendment B, none of the cited references disclose or suggest this limitation of the claims. Hence, independent Claim 1 and those claims dependent thereon are patentable over the cited references.

For similar reasons, the other claims are also patentable over the cited references.

III. Conclusion

For at least the above-stated reasons and the reasons explained in Amendment B, it is respectfully submitted that the claims of the present application are in an allowable form and are patentable over the cited references. Accordingly, it is requested that the application now be allowed.

If any fee should be due for this response, please charge our deposit account 50/1039.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,

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